UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/542,935	04/04/2000	Maria Palasis	02844/56301	5876

26646 7590 03/06/2006

KENYON & KENYON LLP
ONE BROADWAY
NEW YORK, NY 10004

EXAMINER	
WHITEMAN, BRIAN A	

ART UNIT	PAPER NUMBER
1635	

DATE MAILED: 03/06/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/542,935	PALASIS, MARIA	
	Examiner	Art Unit	
	Brian Whiteman	1635	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *01 February 2006*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *60,62,65-91* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *60,62,65-91* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Non-Final Rejection

Claims 60, 62, and 65-91 are pending.

A request for continued examination under 37 CFR 1.114 was filed in this application after appeal to the Board of Patent Appeals and Interferences, but prior to a decision on the appeal. Since this application is eligible for continued examination under 37 CFR 1.114 and the fee set forth in 37 CFR 1.17(e) has been timely paid, the appeal has been withdrawn pursuant to 37 CFR 1.114 and prosecution in this application has been reopened pursuant to 37 CFR 1.114. Applicant's submission filed on 2/1/06 has been entered.

Applicant's traversal, the amendment to claims 60 and 62, and the addition of claims 65-91 is acknowledged and considered by the examiner.

Priority

Applicant has not complied with one or more conditions for receiving the benefit of an earlier filing date under 35 U.S.C. 120 as follows:

The later-filed application must be an application for a patent for an invention which is also disclosed in the prior application (the parent or original nonprovisional application or provisional application); the disclosure of the invention in the parent application and in the later-filed application must be sufficient to comply with the requirements of the first paragraph of 35 U.S.C. 112. See *Transco Products, Inc. v. Performance Contracting, Inc.*, 38 F.3d 551, 32 USPQ2d 1077 (Fed. Cir. 1994).

Instant claims 60, 62, and 65-91 are unsupported under 35 U.S.C. 112, first paragraph, as failing to comply with the 112 first paragraph written description.

The original specification (09/204,254 filed 12/3/98, now US 6,369,039) did not disclose making and using a medical device comprising a biocompatible structure carrying a genetic material, said biocompatible structure comprising an angiogenic agent selected from acidic fibroblast growth factor, basic fibroblast growth factor, vascular growth factor, epidermal growth factor, transforming growth factor alpha and beta, platelet-derived growth factor, and platelet-derived growth factor. However, the list set forth in the new claims does not include all of the products listed in the specification that are considered angiogenic agents (e.g., hif-1). The specification does not disclose the subgenus set in the new claims and claims dependent therefrom. Thus, nothing in the specification would lead one to the particular combination set forth in the amended and claims dependent therefrom and new claims. "It is not sufficient for purposes of the written description requirement of Section 112 that the disclosure, when combined with the knowledge in the art, would lead one to speculate as to modifications that the inventor might have envisioned, but failed to disclose." *Lockwood v. American Airlines Inc.*, 41 USPQ2d 1961, 1966 (CAFC 1997).

Thus, the instant claims 3, 10-12, 17-20, 23-25, 27, 34-38, 42-44, 54-55, 58-60 and 62-64 in the application do not enjoy priority to application '254 filed on 12/3/98.

Applicant's arguments filed 9/2/04 have been fully considered but they are not persuasive.

In response to applicant's argument that the original description of the '039 patent provides written description of a therapeutic agent and a vector encoding a polypeptide or protein

selected from the above recited groups, as claimed, the argument is not found persuasive because the applicant selects some polypeptides from the list and excludes other polypeptides in the specification of the '039 patent. See Purdue Pharma L.P. v. Faulding Inc. 230 F.3d 1320, 1326, 56 USPQ2d 1481, 1486 (Fed. Cir. 2000) noting that "with respect In re Ruschig 379 F.2d 990, 154 USPQ 118 (CCPA 1967) that Ruschig makes clear that one cannot disclose a forest in the original application, and then later pick a tree out of the forest and say "here is my invention." In order to satisfy written description requirement, the blaze marks directing the skilled artisan to that tree must be in the originally filed disclosure." This is the case here, the applicant did not disclose using a list of angiogenic agents excluding hif-1, NOS and any other angiogenic agent listed in the instant specification from the subgenus listed in the instant claims.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 60, 62, and 65-91 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter, which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

New Matter rejection:

Amended claims 60 and 62 and new claims 65-91 filed on 2/1/06/04 introduce new subject matter into the application.

With respect to the limitation 'a therapeutic agent, wherein said therapeutic agent is an angiogenic agent and a vector containing a polynucleotide that established a gene expression sufficient to produce a therapeutically sufficient amount of one or more products encoded by said polynucleotide, wherein said polynucleotide encodes a polypeptide or protein, wherein said polypeptide or protein is an angiogenic agent' in amended claims 60 and 62 and claims dependent therefrom, the original specification did not disclose the limitation. The asserted support cited for the limitation in the claims does not provide support for the limitation. Page 18, lines 18-22 is directed to the angiogenic agents listed in the dependent claims. However, the specification discloses that either the first or the second polynucleotide or both encode the angiogenic agents. There is no disclosure in the specification of an angiogenic agent and a polynucleotide encoding an angiogenic agent. In addition, page 17, line 20 through page 18, line 16 lists several angiogenic agents that are excluded from the instant claims. The instant specification does not disclose the subgenus set forth in the new claims. It is apparent that the applicants at the time the invention was made did not intend or contemplate making and/or using the medical device set forth in the amended claims and newly added claims as part of the disclosure of their invention. There is no evidence in the specification that the applicants were possession of the medical device as set forth in the newly filed claims and amended claims, as it is now claimed, at the time the application was filed.

Applicant's arguments filed 2/1/06 have been fully considered but they are not persuasive.

In response to applicant's argument that the combination of angiogenic agent and a polynucleotide encoding an angiogenic agent is disclosed in the specification (page 5, lines 6-7 and page 6, line 9), the argument is not found persuasive because both pages are directed to a general description of the claimed invention that does not disclose using a first polynucleotide comprising an angiogenic agent and an angiogenic agent. See *Lockwood v. American Airlines Inc.,*.

In response to the applicant's argument that page 18, line 1 and original claims 26 and 33 provide support for the claimed invention, the argument is not found persuasive because page 18 discloses using a first or second polynucleotide encoding an angiogenic and anti-angiogenic agents and not 1) a polynucleotide encoding an angiogenic agent and 2) an angiogenic protein. This is the same reason for why original claims 26 and 33 do not support the claims.

In response to applicant's argument that in view of page 22, line 21 to page 23, line 6, the skilled person would recognize that the invention was designed to increase blood flow and thereby oxygen delivery to tissues by using "angiogenic agents", the argument is not found persuasive because there is no correlation between using a genus of angiogenic agents and using a particular combination comprising an angiogenic agent and a nucleic acid encoding an angiogenic agent that were not disclosed in the instant specification. See *Lockwood v. American Airlines Inc.*.

In response to applicant's argument that although Example 7 on pages 28-29 discloses using two genetic therapeutic agents, the Example clearly directs the skilled person to the concept of practicing the invention wherein both therapeutic agents are "angiogenic agents", the argument is not found persuasive because there is no correlation between using a genus of

angiogenic agents and using an angiogenic agent and a nucleic acid encoding an angiogenic agents. See Purdue Pharma L.P. v. Faulding Inc. 230 F.3d 1320, 1326, 56 USPQ2d 1481, 1486 (Fed. Cir. 2000).

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* v. *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

Claims 60, 62, 65, 67, 68, 69, 71, 72, 73, 75, 77-80, 82-84, 86, 87, 88, 90, and 91 are rejected under 35 U.S.C. 103(a) as being unpatentable over Roth (US 5,879,713) taken with Crystal et al. (US 5,869,037). Roth teaches delivering to a vascular system of an animal a biodegradable, biocompatible polymeric microparticles comprising biologically active molecules selected from the group consisting of growth factors, cytokines, angiogenesis factors, immunosuppressant molecules, peptide fragments thereof and nucleic acid constructs capable of synthesizing these compounds, wherein restenosis has occurred following balloon angioplasty

(abstract and columns 10 and 16-18). Roth teaches the limitation in instant claims 78 and 79 (columns 10 and 16-18). The growth factors can be VEGF, bFGF, and PDGF and DNA encoding them (column 10). The biologically active molecules, which are immobilized on the polymeric microparticles can include proteins, nucleic acid molecules, carbohydrates, lipids and combinations thereof (column 9). Roth teaches the limitation in instant claim 67 (columns 3-4). Roth teaches the limitation in instant claim 68 (column 11). Roth teaches the limitation in instant claims 69 and 84 (column 11). However, Roth does not specifically teach using a nucleic acid encoding an angiogenic agent and an angiogenic agent in the microparticles.

However, at the time the invention was made, Crystal teaches composition comprising a viral vector comprising a nucleic acid encoding a VEGF polypeptide (column 11). Crystal teaches that the composition can be formulated into preparations in solids (column 11). Crystal further teaches that the vector can be delivered with other means of stimulating angiogenesis such as treatment with other angiogenic growth factors (column 11). One of ordinary skill in the art understands that adenovirus provides an efficient means for transferring biological materials to target cells (columns 1 and 2).

It would have been *prima facie* obvious to a person of ordinary skill in the art at the time the invention was made to combine the teaching of Roth taken with Crystal, namely to produce a medical device comprising a polymeric coating comprising a vector comprising a polynucleotide encoding an angiogenic agent and an angiogenic agent. One of ordinary skill in the art would have been motivated to combine the teaching to enhance the circulation where there has been vascular occlusion. See also In re Kerkhoven, 626 F.2d 846, 850, 205 USPQ 1069, 1072 (CCPA 1980).

In addition, it would have been *prima facie* obvious to a person of ordinary skill in the art at the time the invention was made to combine the teaching of Roth taken with Crystal, namely to use the medical device to treat restenosis in a patient. One of ordinary skill in the art would have been motivated to combine the teaching to deliver the agents in a controlled and sustained manner as exemplified by Roth (column 2).

In addition, it would have been *prima facie* obvious to a person of ordinary skill in the art at the time the invention was made to combine the teaching of Roth taken with Crystal, namely to use an adenovirus in the medical device for treating a patient with restenosis. One of ordinary skill in the art would have been motivated to combine the teaching to improve the delivery of the nucleic acid to the cells of interest as exemplified by Crystal (columns 1 and 2).

Therefore the invention as a whole would have been *prima facie* obvious to one ordinary skill in the art at the time the invention was made.

In response to applicant's argument that Roth does not disclose a polymeric coating on a medical device, the argument is not found persuasive because Roth teaches loading the polymeric coating comprising the therapeutic agents onto a stent, which would indicate to the skilled artisan that the teaching of Roth would read on coating on a medical device.

Applicant's arguments with respect to claims 67, 68, 69, 71, 72, 73, 75, 77-80, 82-84, 86, 87, 88, 90, and 91 have been considered but are moot in view of the new ground(s) of rejection.

Claims 60, 62, 65, 66, 80, and 81 are rejected under 35 U.S.C. 103(a) as being unpatentable over Roth et al. taken with Crystal et al. as applied to claims 60, 62, 65, 67, 68, 69,

71, 72, 73, 75, 77-80, 82-84, 86, 87, 88, 90, and 91 above, in further view of Branellec et al. (US Patent No. 5,851,521, cited on a previous PTO-892).

However, Roth and Crystal do not specifically making and using a viral vector (AAV) to deliver the nucleic acid.

However, at the time the invention was made, replication defective AAV viral vectors were well known to one of ordinary skill in the art for delivering nucleic acid to cells using a catheter and using micro-particles (e.g. polylactide) to deliver said nucleic acid (column 9, line 60-column, line 67). Branellec teaches using AAV vectors comprising a protein in a method inhibiting restenosis in a mammal (abstract and column 7, lines 55-65). AAV vectors are able to infect a wide spectrum of cells without inducing any effect on cellular growth, morphology, or differentiation and they do not appear to be involved in human pathologies.

It would have been *prima facie* obvious to a person of ordinary skill in the art at the time the invention was made to combine the teaching of Roth taken with Crystal in further view of Branellec, namely to produce the microparticle comprising a replication defective AAV vector. One of ordinary skill in the art would have been motivated to combine the teaching and make the microparticle comprising a replication defective AAV vector because AAV vectors are well known to one of ordinary skill in the art to be non-pathogenic in vivo and infect a wide spectrum of cells without inducing any effect on cellular growth, morphology, or differentiation.

In addition, it would have been *prima facie* obvious to a person of ordinary skill in the art at the time the invention was made to combine the teaching of Roth taken with Crystal in further view of Branellec, namely to use a replication defective AAV vector in the microparticle for delivering a genetic material to a mammal. One of ordinary skill in the art would have been

motivated to combine the teaching and use the replication defective AAV in the method because AAV vectors are non-pathogenic in mammals and are well known to one of ordinary skill in the art for delivering a nucleic acid to a mammal with restenosis as exemplified by Branellec (column 7).

Therefore the invention as a whole would have been *prima facie* obvious to one ordinary skill in the art at the time the invention was made.

Applicant's arguments with respect to claims 60 and 62 have been considered but are moot in view of the new ground(s) of rejection.

Claims 60, 62, 69, 70, 84, and 85 are rejected under 35 U.S.C. 103(a) as being unpatentable Roth et al. taken with Crystal et al. as applied to claims 60, 62, 65, 67, 68, 69, 71, 72, 73, 75, 77-80, 82-84, 86, 87, 88, 90, and 91 above, and further in view of with Donovan et al. (US 5,833,651, cited on a previous PTO-892).

However, Roth and Crystal do not specifically making and using a metallic stent to deliver the vector and the angiogenic agent.

However, at the time the invention was made, Donovan teaches that metallic stents are well known to one of ordinary skill in the art for delivering microparticles to an area of a mammal (columns 5-6).

It would have been *prima facie* obvious to a person of ordinary skill in the art at the time the invention was made to combine the teaching of Roth taken with Crystal in further view of Donovan, to make a metallic stent comprising the microparticle. One of ordinary skill in the art would have been motivated to combine the teaching, as a matter of designer's choice, and make

a metallic stent comprising the microparticle because metallic stents are well known to one of ordinary skill in the art for delivering a microparticle to an area of a mammal as exemplified by Donovan (columns 5-6).

In addition, it would have been *prima facie* obvious to a person of ordinary skill in the art at the time the invention was made to combine the teaching of Roth taken with Crystal in further view of Donovan, namely to use a metallic stent for delivering the microparticle to an area of a mammal. One of ordinary skill in the art, as a matter of designer's choice, would have been motivated to combine the teaching and use a metallic stent in the method because metallic stents are well known to one of ordinary skill in the art for sustainable delivery of microparticles to an area of a mammal as exemplified by Donovan (columns 5-6).

Therefore the invention as a whole would have been *prima facie* obvious to one ordinary skill in the art at the time the invention was made.

Applicant's arguments with respect to claims 60 and 62 have been considered but are moot in view of the new ground(s) of rejection.

Claims 60, 62, 74, 76, and 89 are rejected under 35 U.S.C. 103(a) as being unpatentable over Roth taken with Crystal as applied to claims 60, 62, 65, 67, 68, 69, 71, 72, 73, 75, 77-80, 82-84, 86, 87, 88, 90, and 91 above, and further in view of Isner (US 5,652,225).

However, Roth taken with Crystal do not specifically teach using PEGF and TGF alpha or TGF beta.

However, at the time the invention was made, PEGF, TGF-alpha and TGF beta were known to one of ordinary skill in the art as angiogenic proteins as taught by Isner. See column 3.

It would have been *prima facie* obvious to a person of ordinary skill in the art at the time the invention was made to combine the teaching of Roth and Crystal in further view of Isner, namely to use PEGF in the method. One of ordinary skill in the art would have been motivated to combine the teaching because PEGF is a growth factor that can be used to induce angiogenesis in a patient.

In addition, it would have been *prima facie* obvious to a person of ordinary skill in the art at the time the invention was made to combine the teaching of Roth and Crystal in further view of Isner, namely to use either TGF alpha or TGF beta in the method. One of ordinary skill in the art would have been motivated to combine the teaching because TGF alpha and TGF beta are growth factors that can be used to induce angiogenesis in a patient.

Therefore the invention as a whole would have been *prima facie* obvious to one ordinary skill in the art at the time the invention was made.

Applicant's arguments with respect to claims 60 and 62 have been considered but are moot in view of the new ground(s) of rejection.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Brian Whiteman whose telephone number is (571) 272-0764. The examiner can normally be reached on Monday through Friday from 7:00 to 4:00 (Eastern Standard Time), with alternating Fridays off.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Andrew Wang, acting SPE – Art Unit 1635, can be reached at (571) 272-0811.

Papers related to this application may be submitted to Group 1600 by facsimile transmission. Papers should be faxed to Group 1600 via the PTO Fax Center. The faxing of such papers must conform with the notice published in the Official Gazette, 1096 OG 30 (November 15, 1989). The Fax Center number is (571) 273-8300.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to (571) 272-0547.

Patent applicants with problems or questions regarding electronic images that can be viewed in the Patent Application Information Retrieval system (PAIR) can now contact the USPTO's Patent Electronic Business Center (Patent EBC) for assistance. Representatives are available to answer your questions daily from 6 am to midnight (EST). The toll free number is (866) 217-9197. When calling please have your application serial or patent number, the type of document you are having an image problem with, the number of pages and the specific nature of the problem. The Patent Electronic Business Center will notify applicants of the resolution of the problem within 5-7 business days. Applicants can also check PAIR to confirm that the problem has been corrected. The USPTO's Patent Electronic Business Center is a complete service center supporting all patent business on the Internet. The USPTO's PAIR system provides Internet-based access to patent application status and history information. It also enables applicants to view the scanned images of their own application file folder(s) as well as general patent information available to the public.

For all other customer support, please call the USPTO Call Center (UCC) at 800-786-9199.

Brian Whiteman
Patent Examiner, Group 1635

BRIAN WHITEMAN
PATENT EXAMINER